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CITATION:

NAGASE, MASAO ...[et al]. Surgery of the Parathyroid Gland. 日本外科宝
函 1978, 47(6): 704-710

ISSUE DATE:

1978-11-01

URL:

<http://hdl.handle.net/2433/208305>

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Surgery of the Parathyroid Gland

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Received for Publication Sept., 11, 1978

Introduction

Surgical operations for primary hyperparathyroidism are increasingly done in the United States and will be so in Japan.

A case of primary hyperparathyroidism cured by extirpation of an adenoma will be presented briefly and some mentions will be made on intriguing points in the parathyroid surgery.

Case report

A 51 year old man was admitted to our hospital because of polydipsia, pains in the knees and ankles and recurrent bouts of nephrolithiasis; urinary stone deliveries four times during the last ten years.

Laboratory findings: Positive findings were as follows: serum calcium 10.8-12.9mg/dl, inorganic phosphorus 2.0mg/dl, alkaline phosphatase 368U/ml, parathyroid hormone in the peripheral blood 1.6ng/dl (normal is less than 0.5ng/dl). Short QT intervals in ECG. A calcium shadow in the left kidney on abdominal plain film. Subperiosteal resorption of bones of fingers (Fig.1).

The parathyroid scintigram using ^{201}Tl showed a hot spot in the right lower region of the neck (Fig. 2).

Operative findings: A collar incision as for subtotal thyroidectomy was used. Behind the lower pole of the right thyroid lobe was found a tumor measuring $2.7 \times 2.0 \times 1.4\text{cm}$, which was extirpated without injuring the recurrent laryngeal nerve. (Figs. 3 and 4). The other three glands were identified and observed as being normal-sized. A part of the right superior glands was excised and diagnosed microscopically as normal parathyroid gland by frozen section. The excised tumor was an adenoma of the parathyroid gland (Fig.5).

Postoperative course: He was given orally calcium lactate 12g/day, dihydrotachysterol 1mg/day and ergocalciferol 112,000U/day from the next day on. About 48 hours after the surgery, he began to complain of paresthesia around the mouth and of the fingers and

Key words : Primary hyperparathyroidism, Multiple endocrine adenomatosis.

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Fig. 1 Subperiosteal resorption of bones.

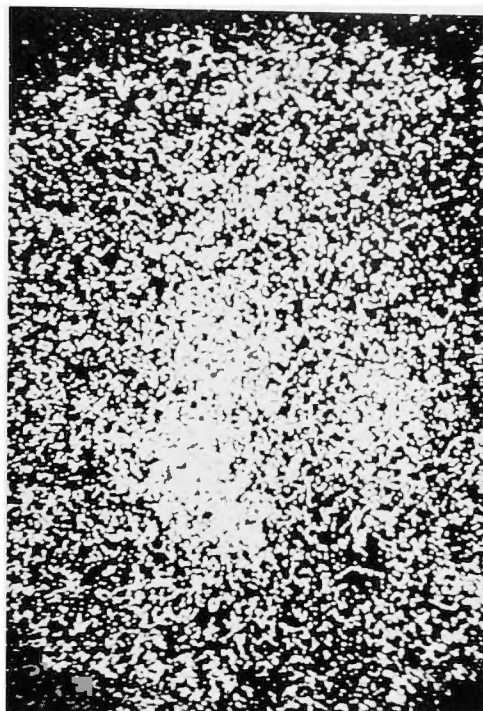


Fig. 2 Scintigram with ^{201}Tl

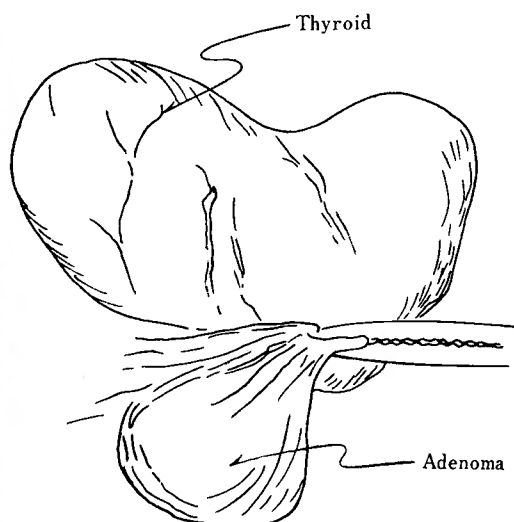
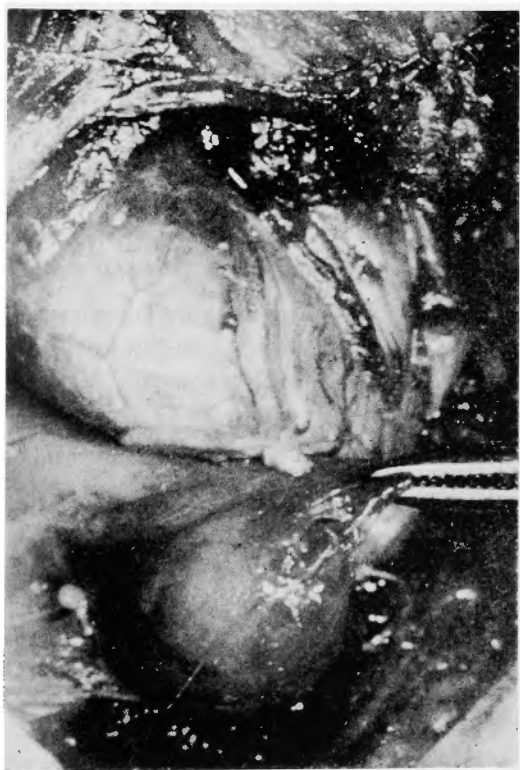


Fig. 3 Operative finding



Fig. 4 Parathyroid adenoma

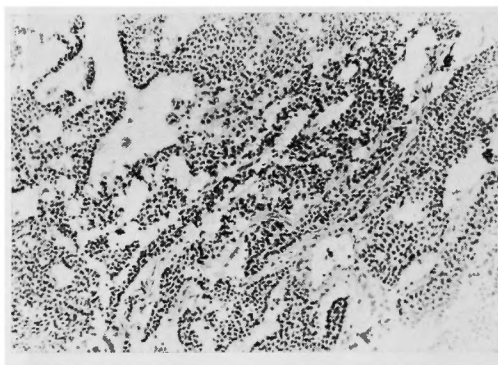


Fig. 5 Histology of the adenoma

became dyspnoic. His serum calcium was 9.0mg/dl at that time. Intravenous drip infusion of 8.5 percent solution of calcium gluconate was begun and the above symptoms disappeared after the infusion of 100ml of the solution. Thereafter, his postoperative course was quite uneventful, serum calcium being maintained at 10.5 to 10.8 mg/dl. He was given only calcium lactate 6g/day orally from the 10th postoperative day on and was discharged on the 20th postoperative day.

Discussion

Pathology: Patients with primary hyperparathyroidism are increasingly found through the increased use of multichannel biochemical screenings in general medical practice. Boonstra and Jackson found proved hyperparathyroidism in one of every 834 patients (0.12 percent) when serum calcium was measured routinely²⁾. Fujimoto in our country has reported that he found out the disease in one of every 5,000 patients⁵⁾.

Females are affected more frequently than males, the reported ratio being 3 to 2¹¹⁾ or 2 to 1⁸⁾¹²⁾¹³⁾¹⁴⁾. Although the disease may be seen in any ages, adults from 30 to 60 years old are commonly affected⁸⁾¹²⁾.

There are many arguments and even confusions regarding the pathology of the parathyroid gland causing hyperparathyroidism. Ten years ago, according to EDIS et al³⁾, it was generally accepted that solitary adenomas comprised approximately 80 percent of cases and chief cell hyperplasia approximately 20 percent. At present, many authors report dramatically increased incidence of chief cell hyperplasia. FUJIMOTO⁴⁾ has stated that patients with mild hypercalcemic symptoms are increasingly found by biochemical examinations, and that the most frequent lesion is unequal hyperplasia, the second is equal hyperplasia, the third is adenoma and the least is cancer. The Group from the Massachusettes General Hospital, on the other hand, has reported that single parathyroid adenoma still accounts for 80 percent of the cases of primary hyperparathyroidism¹⁶⁾. According to JUNGIGNER's⁶⁾ review, pathological lesions in primary hyperparathyroidism are as shown in Table 1.

Table 1 Pathological lesions in primary hyperparathyroidism⁶⁾

	Romanus 1973 n=274	Chiu and Wang 1971 n=431	Straus 1969 n=58	Hoehn 1969 n=724	Junginger & Meisner 1977 n=73
Solitary adenoma	79.2%	79%	46%	89%	59%
Multiple adenoma	1.8%	3%	7%	1%	6%
Hyperplasia water clear cell	5.1%	4%	9%	2%	—
Chief cell hyperplasia	3.6%	10%	10%	4%	26%*
Adenoma and hyperplasia	6.2%	—	24%	—	8%
Carcinoma	—	4%	4%	1%	1%

* dominant cell type

Table 2 Frequency of persistent hypercalcemia after operations for primary hyperparathyroidism⁶⁾

Author		Number of operated patients	Persistent hypercalcemia	
			after 1 operation	after 2 or more operations
Thoren	1969	78	2 (2.6%)	
Pridgen	1969	30	1 (3.3%)	
Lessen	1968	83	8 (9.6%)	
Purnell	1971	171	20 (10.8%)	
Haff	1970	47	8 (17.0%)	
Latimer	1972	35	6 (17.1%)	4 (11.4%)
Rienhoff	1968	102	19 (18.6%)	13 (13.4%)
Hellstroem	1957	92	20 (22.0%)	6 (6.5%)
Blalock	1971	79	18 (22.8%)	
Junginger	1960-1974	90	17 (18.8%)	

BLACK et al¹¹⁾ have stated that chief cell hyperplasia and adenoma cannot be differentiated by any technique short of electron microscopy. In view of the current states of our knowledge on pathology of the parathyroid gland, every surgeon should explore all four glands, even when he has found out an adenoma.

Localization studies: Preoperative localization of parathyroid lesions may be not infrequently difficult because of their small size and location.

Parathyroid scanning with selenomethionine, selective arteriography through the thyroid artery and internal mammary artery, and measurement of parathyroid hormone concentration in blood samples obtained by selective catheterization from the thyroid veins have been advocated for localization studies. All these methods are not of so much diagnostic accuracy and not so much easy to perform as to be used routinely for all patients and are reserved for localization study in the recurrent cases which are seen in 2.6% to 22.8% after the first operation as summarized by JUNGINGER et al (Table 2)⁶⁾.

During the surgery, intravenous injection of methylene blue or toluidine blue-O solution is used to stain the gland¹⁵⁾. KATO⁷⁾ has recommended to administer the dye in small amount through the subclavian artery in order to avoid the cardiotoxic effect of the dye. According to Junginger's review, location of parathyroid adenoma in 749 patients are as

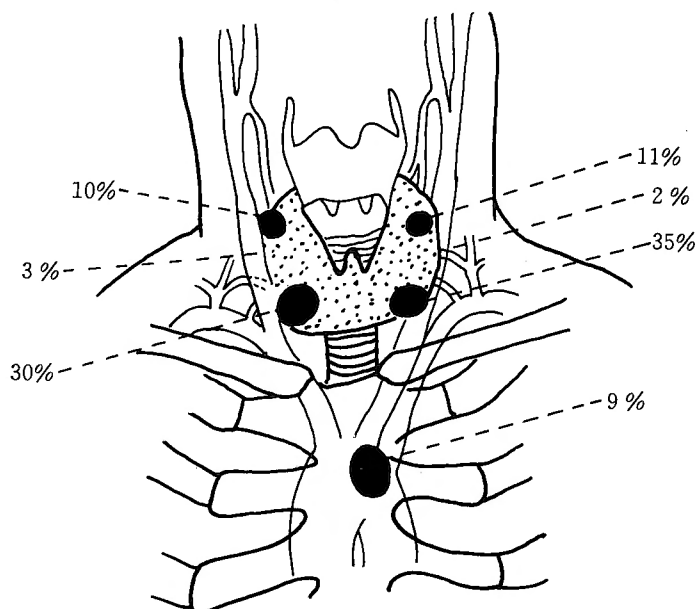


Fig. 6 Location of parathyroid adenomas in 749 patients⁶⁾.

shown in Fig.6.

As mentioned above, differentiation between adenoma and hyperplasia is sometimes difficult both macroscopically and microscopically. If multiple glands are suspected to be affected, subtotal parathyroidectomy removing three glands and half the last one gland should be done. In this event, the resected parathyroids are preferably preserved in frozen condition, and are autotransplanted into the muscles after dicing to pieces of 1×1 mm when permanent hypoparathyroidism ensues³⁾.

Among 62 ectopic parathyroid adenomas reported by Satava¹³⁾, 43 adenomas were in the tracheoesophageal groove, 9 in the anterior mediastinum, 4 in the thymus, and 4 in the thyroid. When no abnormal parathyroid gland could be found by thorough exploration of the neck, it has been recommended to postpone the further exploration to three weeks or four weeks later. However, FUJIMOTO⁵⁾ and Rothmund et al. have suggested to perform mediastinotomy at the first operation.

Postoperative tetany: Serum calcium level falls rather abruptly to normal or subnormal range within 24 hours after successful surgery. Postoperative tetany may occur as a result of 1) depression of the remaining glands by the overactive adenoma, 2) deposition of calcium in the depleted bones and 3) devascularization of the remnant parathyroid. Moreover, it should be recognized that transient tetany may occur, even when the serum calcium has fallen only to near normal range, until the patient becomes accustomed to the low level¹⁰⁾. Our case complained of paresthesia and mild dyspnea with the serum calcium level of 9.0mg/dl 48 hours after surgery and was relieved by intravenous infusion of

calcium.

Secondary and tertiary hyperparathyroidism: Secondary hyperparathyroidism with chief cell hyperplasia is caused by hypocalcemia due mainly to chronic renal insufficiency and sometimes to severe chronic intestinal malabsorption. Its treatment is nonsurgical.

If secondary hyperparathyroidism lasts for a long period of time, parathyroid hyperfunction may become more or less autonomous and hypercalcemia may ensue, and parathyroidectomy may be indicated for a few cases refractory to medical treatments.

The secondary and tertiary hyperparathyroidism are becoming more important diseases in accordance with the increasing use of artificial kidney and kidney transplantation.

Multiple endocrine adenomatosis (MEA): Primary hyperparathyroidism may be a component of multiple endocrine adenomatosis. In MEA-type 1 the parathyroid is affected in combination with islet cells of the pancreas and with the anterior pituitary, and in MEA-type 2 in combination with C-cells of the thyroid and with the adrenal medulla.

A series of cells originating from the ectodermal neural crest have ability to secrete polypeptid hormones and are called APUD cells because of their common biochemical characteristics (fluorogenic Amine content, amine Precursor Uptake and amino acid Decarboxylase). The cells belonging to this series are islet cells of the pancreas, ACTH secreting cells of the anterior pituitary, C-cells of the thyroid, cells of the adrenal medulla, enterochromaffine cells and so on.

Induction of the concept of APUD cells has partly clarified the pathogenesis of MEA. Parathyroid gland is, however, of endodermal origin, and whether its participation in MEA is primary or secondary is still unsettled. Anyway, in every patient with primary hyperparathyroidism, all the other glands should be examined.

Summary

A case of primary hyperparathyroidism due to an adenoma is reported. Intriguing points in parathyroid surgery are discussed. Some mentions are made on secondary and tertiary hyperparathyroidism and on multiple endocrine adenomatosis.

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和文抄録

副 甲 状 腺 の 外 科

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原発性副甲状腺機能亢進症を呈する51才の男性に対して、手術を行ない、右下副甲状腺から発生した腺腫を切除することによって治癒させ得た。その概略を報告すると共に、原発性副甲状腺機能亢進症の病理、病

変所在部位の診断法、手術方針、術後合併症などについて述べ、更に、二次性、三次性副甲状腺機能亢進症及び多発性内分泌腺症 (multiple endocrine adenomatosis) についても言及した。